AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in this application.

Listing of Claims:

1. (withdrawn) A crystalline DMSO solvate of gatifloxacin characterized by at least one characteristic selected from:

a) x-ray reflections at about 14.7, 16.3, 17.6, and 19.7° ± 0.2° θ, and

b) endothermic peaks at about 133° and about 167° C in DSC.

2. (withdrawn) The crystalline DMSO solvate of gatifloxacin of claim 1 characterized by x-ray reflections at about 14.7, 16.3, 17.6, and 19.7° ± 0.2° θ.

3. (withdrawn) The crystalline DMSO solvate of gatifloxacin of claim 2 further characterized by x-ray reflections at about 8.2, 13.1,20.3,21.2, and 23.0° ± 0.2° θ.

4. (withdrawn) The crystalline DMSO solvate of claim 3 having an x-ray diffraction diagram substantially as shown in Figure 1.

5. (withdrawn) The crystalline DMSO solvate of gatifloxacin of claim 1 characterized by endothermic peaks at about 133° and about 167° C in DSC.

6. (withdrawn) The crystalline DMSO solvate of claim 5 having a. DSC thermogram substantially as shown in Figure 14.

7. (withdrawn) The crystalline DMSO solvate of claim 1 having a DMSO content of about 20% to about 27% by weight.

8. (withdrawn) A crystalline DMSO solvate of gatifloxacin characterized by:

a) x-ray reflections at about 14.7,16.3, 17.6, and 19.7° ± 0.2° θ, and

b) endothermic peaks at about 133° and about 167' C in DSC.

9. (withdrawn) A crystalline DMSO solvate of gatifloxacin characterized by at least one characteristic selected from:

a) x-ray reflections at about 6.5, 14.6, 17.4, and 19.4° ± 0.2° θ, and

b) endothermic peaks at about 122° and about 137° in DSC.

10. (withdrawn) The crystalline DMSO solvate of gatifloxacin characterized by x-ray reflections at about 6.5, 14.6, 17.4, and 19.4° ± 0.2° θ.

11. (withdrawn) The crystalline DMSO solvate of gatifloxacin of claim 10 further characterized by x-ray reflections at about 9.1,9.7, 10.5, 12.3,12.8, 15.3, 18.2, 19.9,20.3,20.9, and 23.0° ± 0.2° 2θ.

12. (withdrawn) The crystalline DMSO solvate of claim 11 having an x-ray diffraction diagram substantially as shown in Figure 2.

13. (withdrawn) The crystalline DMSO solvate of claim 9 characterized by endothermic peaks at about 122° and about 137° in DSC.

14. (withdrawn) The crystalline DMSO solvate of claim 13 having a DSC thermogram substantially as shown in Figure 15.

15. (withdrawn) The crystalline DMSO solvate of claim 9 having a DMSO content of about 25% to about 30% by weight.

16. (withdrawn) A crystalline DMSO solvate of gatifloxacin characterized by:
a) x-ray reflections at about 6.5, 14.6, 17.4, and 19.4° ± 0.2° θ, and
b) endothermic peaks at about 122° and about 137° in DSC.

17. (withdrawn) A crystalline form of gatifloxacin characterized by at least one of
a) x-ray reflections at about 5.2, 11.2, 11.5, i4.3, and 22.2° ± 0.2° θ,
and
b) an endothermic peak at about 178° C in DSC.

18. (withdrawn) The crystalline form of gatifloxacin of claim 17 characterized by x-ray reflections at about 5.2, 1 1.2, 1 1.5, 14.3, and 22.2° ± 0.2° θ.

19. (withdrawn) The crystalline form of gatifloxacin of claim 18 further characterized by x-ray reflections at about 15.5, 16.2, 16.5, 17.0, 17.5,20.4, and 23.2° ± 0.2° θ.

20. (withdrawn) The crystalline form of gatifloxacin of claim 19 having an x-ray diffraction diagram substantially as shown in Figure 3.

21. (withdrawn) The crystalline form of gatifloxacin of claim 17 characterized by an endothermic peak at about 178° C in DSC.

22. (withdrawn) The crystalline form of gatifloxacin of claim 21 having a DSC thermogram substantially as shown in Figure 16.

23. (withdrawn) A crystalline form of gatifloxacin characterized by:

a) x-ray reflections at about 5.2, 1 1.2, 1 1.5, 14.3, and 22.2° ± 0.2° θ,

and

b) an endothermic peak at about 178° C in DSC.

24. (withdrawn) A crystalline form of gatifloxacin characterized by at least one of:

a) x-ray reflections at about 6.6, 7.2, 13.2, 17.6, 19.8, and 23.0° ± 0.2° θ, and

b) an endotherm at about 122°C in DSC.

25. (withdrawn) The crystalline form of gatifloxacin of claim 24 characterized by x-ray reflections at about 6.6, 7.2, 13.2, 17.6, 19.8, and 23.0° ± 0.2° θ.

26. (withdrawn) The crystalline form of gatifloxacin of claim 25 having an x-ray diffraction diagram substantially as shown in Figure 4.

27. (withdrawn) The crystalline form of gatifloxacin of claim 28 characterized by an endotherm at about 122°C in DSC.

28. (withdrawn) The crystalline form of gatifloxacin of claim 27 having a DSC thermogram substantially as shown in Figure 20.

29. (withdrawn) The crystalline form of claim 24 that is a DMSO solvate.

30. (withdrawn) A crystalline form of gatifloxacin characterized by:

a) x-ray reflections at about 6.6, 7.2, 13.2, 17.6, 19.8, and 23° ± 0.2° θ, and

b) an endotherm at about 122°C in DSC.

31. (withdrawn) A crystalline form of gatifloxacin characterized by at least one of:

a) x-ray reflections at about 7.8, 10.8, 13.7, 18.6, and 19.9° ± 0.2° θ,

and

b) endotherms at about 90° and about 175° C in DSC.

32. (withdrawn) The crystalline form of gatifloxacin of claim 3 1 characterized by x-ray reflections at about 7.8, 10.8, 13.7, 18.6, and 19.9° ± 0.2° θ.

33. (withdrawn) The crystalline form of gatifloxacin of claim 32 having an x-ray diffraction diagram substantially as shown in Figure 5.

34. (withdrawn) The crystalline form of gatifloxacin of claim 3 1 characterized by endotherms at about 90° and about 175° C in DSC.

35. (withdrawn) The crystalline form of gatifloxacin of claim 34 having a DSC thermogram substantially as shown in Figure 21.

36. (withdrawn) A crystalline form of gatifloxacin characterized by:

a) x-ray reflections at about 7.8, 10.8, 13.7, 18.6, and 19.9° ± 0.2° θ,

and

b) endotherms at about 90° and about 175° C in DSC.

37. (withdrawn) A crystalline form of gatifloxacin characterized by at least one of

a) x-ray reflections at about 13.4, 14.8, 17.6, 19.6, and 20.0° ± 0.2° θ,

and

b) an endotherm at about 99° C in DSC.

38. (withdrawn) The crystalline form of gatifloxacin of claim 37 characterized by x-ray reflections at about 13.4, 14.8, 17.6, 19.6, and 20.0° ± 0.2° θ.

39. (withdrawn) The crystalline form of gatifloxacin of claim 38 having an x-ray diffraction diagram substantially as shown in Figure 6.

40. (withdrawn) The crystalline form of gatifloxacin of claim 37 characterized by a DSC endotherm at about 99°C.

41. (withdrawn) The crystalline form of gatifloxacin of claim 40 having a DSC thermogram substantially as shown in Figure 22.

42. (withdrawn) The crystalline form of gatifloxacin of claim 37 that is a DMSO solvate.

43. (withdrawn) A crystalline form of gatifloxacin characterized by at least one of
a) x-ray reflections at about 13.9, 14.8, and 16.1° ± 0.2° θ, and
b) endotherms at about 92° and about 188° C in DSC.

44. (withdrawn) The crystalline form of gatifloxacin of claim 43 characterized by x-ray reflections at about 13.9, 14.8, and 16.1° ± 0.2° θ.

45. (withdrawn) The crystalline form of gatifloxacin of claim 44 having an x-ray diffraction diagram substantially as shown in Figure 7.

46. (withdrawn) The crystalline form of gatifloxacin of claim 43 characterized by endotherms at about 92° and about 188° C in DSC.

47. (withdrawn) The crystalline form of gatifloxacin of claim 46 having a DSC thermogram essentially as shown in Figure 23.

48. (withdrawn) A crystalline form of gatifloxacin characterized by:
a) x-ray reflections at about 13.9, 14.8, and 16.1° ± 0.2° θ , and
b) endotherms at about 92° and about 188° C in DSC.

49. (withdrawn) A crystalline form of gatifloxacin characterized by at least one of:
a) x-ray reflections at about 6.7, 9.5, 10.7, 13.1, 17.2° ± 0.2° θ, and
b) endotherms at about 65°, 90°, and 190° C in DSC, wherein the endotherm at 190°C is sharper than the other endotherms.

50. (withdrawn) The crystalline form of gatifloxacin f claim 49 characterized by x-ray reflections at about 6.7, 9.5, 10.7, 13.1, 17.2° ± 0.2° θ.

51. (withdrawn) The crystalline form of gatifloxacin of claim 50 having an x-ray diffraction diagram substantially as shown in Figure 8.

52. (withdrawn) The crystalline form of gatifloxacin of claim 49 characterized by endotherms at about 65 248, 90°, and 190° C in DSC, wherein the endotherm at 190° C is sharper than the other endotherms.

53. (withdrawn) The crystalline form of gatifloxacin of claim 52 having a DSC thermogram substantially as shown in Figure 24.

54. (withdrawn) A crystalline form of gatifloxacin characterized by:

a) x-ray reflections at about 6.7, 9.5, 10.7, 13.1, 17.2° ± 0.2° θ, and

b) endotherms at about 65°, 90°, and 190° C in DSC, wherein the endotherm at 190°C is sharper than the other endotherms.

55. (withdrawn) A crystalline form of gatifloxacin characterized by x-ray reflections at about 5.5, 10.3, 10.8, 13.9, and 15.1° ± 0.2° θ.

56. (withdrawn) The crystalline form of gatifloxacin of claim 55 having an x-ray diffraction diagram essentially as shown in Figure 9.

57. (withdrawn) A crystalline form of gatifloxacin characterized by x-ray reflections at about 7.8, 91, 9.4, and 9.6° ± 0.2° θ.

58. (withdrawn) The crystalline form of gatifloxacin of claim 57 having an x-ray diffraction diagram substantially as shown in Figure 10.

59. (withdrawn) A crystalline form of gatifloxacin characterized by x-ray reflections at about 6.6, 9.9, 10.5, and 12.9° ± 0.2° θ.

60. (withdrawn) The crystalline form of gatifloxacin of claim 59 having an x-ray diffraction diagram substantially as shown in Figure 11.

61. (withdrawn) A crystalline form of gatifloxacin characterized by x-ray reflections at about 6.3, 9.3, 19.3, 20.8, 24.5, and 25.1° ± 0.2° θ.

62. (withdrawn) The crystalline form of gatifloxacin of claim 61 having an x-ray diffraction diagram substantially as shown in Figure 12.

63. (withdrawn) A crystalline form of gatifloxacin characterized by x-ray reflections at 6.4, 9.4, 16.4, 18.9, and 19.2° ± 0.2° θ.

64. (withdrawn) The crystalline form of gatifloxacin of claim 63 having an x-ray diffraction diagram substantially as shown in Figure 13.

65. (currently amended) A method of making ~~a~~ crystalline ~~form of~~ gatifloxacin form CX characterized by at least one of: (i) a powder x-ray diffraction pattern having reflections at about 6.5, 14.6, 17.4, and 19.4°± 0.2° 2θ; and (ii) a differential scanning calorimetry thermogram having endothermic peaks at about 122°C and about 137°C, ~~having at least one characteristic of form CX~~ comprising the steps of:

a) combining an initial solution of gatifloxacin in DMSO with water at a temperature of about 55° C,

b) cooling the combination to a temperature of about 0° C at a ~~coling~~ cooling rate of about 10° per hour whereby a suspension is obtained,

c) isolating the crystalline ~~form of~~ gatifloxacin ~~having at least one characteristic of~~ form CX from the suspension, and

d) washing the isolated crystalline ~~form of~~ gatifloxacin form CX with ~~sufficient~~ acetonitrile ~~to maintain the crystalline form as form CX~~.

66. (currently amended) A method of making ~~a~~ crystalline ~~form of~~ gatifloxacin form CW characterized by at least one of: (i) a powder x-ray diffraction pattern having reflections at about 5.2, 11.2, 11.5, 14.3, and 22.2° ± 0.2° 2θ; and (ii) a differential scanning calorimetry thermogram having an endothermic peak at about 178°C, ~~having at least one characteristic of form CW~~ comprising the steps of:

a) providing crystalline gatifloxacin form CX characterized by at least one of: (i) a powder x-ray diffraction pattern having reflections at about 6.5, 14.6, 17.4, and 19.4°± 0.2° 2θ; and (ii) a differential scanning calorimetry thermogram having endothermic peaks at about 122°C and about 137°C, and

d) drying the crystalline gatifloxacin form CX at reduced pressure for about 8 hours to obtain the ~~crystalline form having at least one characteristic of~~ crystalline gatifloxacin form CW.

67. (currently amended) The method of claim ~~59~~ 66 further comprising the step of, prior to drying, washing the isolated solid gatifloxacin with acetonitrile.

68. (withdrawn – currently amended) A method of making a crystalline form of gatifloxacin having at least one characteristic of form CY comprising the steps of

a) providing an initial solution of gatifloxacin in DMSO at a concentration of at least about 2 M and a temperature of about 40° C,

b) combining the solution with water at a temperature of about 40° C,

c) cooling the solution to a temperature of about 5° C and maintaining the suspension obtained at about 5° C for a holding time,

d) isolating DMSO-wet solid gatifloxacin from the suspension,

e) suspending the isolated DMSO-wet solid gatifloxacin in acetonitrile,

f) isolating the gatifloxacin from the suspension, and

g) drying the isolated gatifloxacin at about 50° C and ~~<<reduced pressure>>~~ reduced pressure for at least about 12 hours.

69. (withdrawn) The method of claim 68 wherein the initial solution of gatifloxacin is provided by concentrating, by distilling-off DMSO under high vacuum (< 5 mm Hg), a solution obtained by reacting 2-methylpiperazine and 1-cyclopropyl-6,7-difluoro1-,4-dihydro-8-methoxy-4-oxo-3-quinolinecarboxylic acid in DMSO solvent.

70. (withdrawn) The method of claim 68 wherein the holding time of step c) is about 20 hours.

71. (withdrawn) A method of making a crystalline form of gatifloxacin having at least one characteristic of form CZ comprising the steps of:

a) providing an initial solution of gatifloxacin in DMSO at about 55°C,

b) combining, at about 55° C, the provided solution with water and toluene, 1:2 to 1:3, vol:vol,

c) cooling the resulting mixture to about 11° C at a cooling rate of about 10° per hour,

d) heating the mixture to about 35° C and maintaining the mixture at this temperature for about 1 hour,

e) cooling the mixture to about 11° C at a cooling rate of about 4° per hour,

f) maintaining the resulting suspension at about 10°C for a holding time,

g) isolating the gatifloxacin having at least one characteristic of form CZ from the suspension obtained, and

h) washing the isolated gatifloxacin with acetonitrile.

72. (withdrawn) The method of claim 71 wherein the holding time of step f) is about 12 hours.

73. (withdrawn) A method of making a crystalline form of gatifloxacin having at least one characteristic of form W comprising the steps of

a) providing, at reflux temperature, a solution of gatifloxacin in acetonitrile,

b) combining, at reflux temperature, the solution with about one-tenth of its volume of polyethylene glycol,

c) cooling the resulting solution to about 57°C and seeding the solution with gatifloxacin hemihydrate,

d) maintaining the seeded solution at about 57° C for about 2 hours,

e) cooling the resulting seeded solution to about 5° C at about 5° per hour,

f) maintaining the resulting suspension at about 5° C for a holding time,

g) isolating crystalline gatifloxacin the suspension,

h) washing the isolated crystalline gatifloxacin with acetonitrile, and

i) drying the isolated, acetonitrile-washed crystalline gatifloxacin to obtain gatifloxacin having at least one characteristic of form W.

74. (withdrawn) The method of claim 73 wherein the holding time of step f) is about 2 hours.

75. (withdrawn) A method of making a crystalline form of gatifloxacin having at least one characteristic of form Y comprising the steps of:

a) providing a slurry of gatifloxacin hydrochloride in a 9:1, vol:vol, mixture of acetonitrile and water at a temperature of about 5° C,

b) combining the suspension with a volume of an aqueous solution of NaOH sufficient to neutralize at least about 70 mole % of the hydrochloride,

c) isolating solid gatifloxacin from the resulting suspension,

d) washing the isolated solid gatifloxacin with a 9: 1, v:v mixture of acetonitrile and water, and

e) drying the isolated solid gatifloxacin at about 50° C and reduced pressure to obtain the crystalline form of gatifloxacin having at least one characteristic of form Y.

76. (withdrawn) The method of claim 75 wherein the drying of step d) is for a time of about 12 hours.

77. (withdrawn) A method of making a crystalline form of gatifloxacin having at least one characteristic of form Z comprising the steps of:

a) providing a hot-filtered solution of gatifloxacin in acetonitrile at about 80°

b) cooling the solution to about 60°C,

c) maintaining the filtered solution at about 60°C for about 1 hour,

d) cooling the solution to about 5° C at a cooling rate of about 20° to about 25° per hour,

e) maintaining the resulting suspension at about 5°C for about 30 minutes,

f) isolating the crystalline form of gatifloxacin having at least one characteristic of form Z from the suspension.

78. (withdrawn) A method of making gatifloxacin in crystalline form CHI comprising the step of heating gatifloxacin having at least one characteristic of form CY at about 100° C for at least about 30 minutes.

79. (withdrawn) A method of making gatifloxacin crystalline form RH comprising the step of heating gatifloxacin form R at about 50°C to about 70°C.

80. (withdrawn) A method of making gatifloxacin crystalline form V comprising the step of heating gatifloxacin crystalline form CZ at about 110° C to about 130°C.

81. (withdrawn) A method of making gatifloxacin in crystalline form T2RP comprising the step of heating gatifloxacin crystalline form CW at about 135°C to about 150°C.

82. (withdrawn) A method of making gatifloxacin in crystalline form HX1 comprising the steps of

a) suspending, at ambient temperature, DMSO-wet gatifloxacin,

b) maintaining the suspension at ambient temperature for about 1 hour,

and

c) isolating gatifloxacin crystalline form HX1 from the suspension.

83. (withdrawn) A method of making gatifloxacin in crystalline form HX2 comprising the steps of slurrying, at ambient temperature, gatifloxacin in water, at about 20% weight-to-volume, and isolating gatifloxacin in crystalline form HX2 from the suspension.

84. (withdrawn) A pharmaceutical formulation comprising at least one pharmaceutically acceptable excipient and at least one crystalline form of gatifloxacin having at least one characteristic of a crystalline form of gatifloxacin selected from forms CW, CX, CY, CZ, W, X, Y, Z, CHI, CH2, RH, HX1, and HX2.